

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: King, K. *et al.*

Serial No.: Request for Continued Prosecution of  
USSN 09/752,145

Filed: Herewith

For: *EXPRESSION OF G PROTEIN COUPLED  
RECEPTORS IN YEAST*

Attorney Docket No.: 50370-60735DIV (formerly  
CPI-013CNDV4RCE)

Group Art Unit: 1645

Examiner: Ulm, John D.

**Mailstop Box RCE**

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Peter C. Lauro, Esq.

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**INFORMATION DISCLOSURE STATEMENT**

Dear Sir:

For the Examiner's convenience in reviewing this application, Applicants submit a consolidated PTO Form 1449, listing all references cited during the prosecution of the parent applications. The present application is a Request for Continued Prosecution of U.S. Serial No. 09/752,145, filed December 29, 2000 (formerly Atty. Docket No. CPI-013CNDV4RCE). The majority of the references listed on the enclosed PTO Form 1449 have been previously cited by

or submitted to the Office in the prior application, and, in accordance with 37 CFR §1.98(d), copies of references A1-G8 are not enclosed, but will be provided upon request.

The remaining references H1-H4 have not been previously cited and are enclosed herewith. In particular, reference H3, a published Japanese patent application, was cited during prosecution of corresponding Japanese patent application 515,188/1991, now issued as Japanese Patent 3,348,406, and of corresponding pending Japanese divisional patent application 57,831/2002. References H3 and H4 (also a published Japanese patent application) were also cited during prosecution of corresponding pending Japanese divisional patent application 311,757/2003. English abstracts are attached to each of references H3 and H4. In addition, references H1 and H2 are the corresponding U.S. patents that issued from the U.S. priority applications for references H3 and H4, respectively.

Finally, reference H5 was also cited during prosecution of corresponding Japanese patent application 515,188/1991, now issued as Japanese Patent 3,348,406, and of corresponding pending Japanese divisional patent application 57,831/2002. Although reference H5 *per se* was not made of record in prior applications, references A11 and B6, the corresponding PCT international application and U.S. patent that issued from the priority application for reference H5, respectively, were made of record in the prior application. The Examiner will note that references A11 and B6 are indicated on the cover page of reference H5.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understands that the Examiner will make an independent evaluation of the cited publications.

Under 37 CFR § 1.97(b)(1), no additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. No.04-1105.

Respectfully submitted,  
EDWARDS & ANGELL, LLP

By 

Peter C. Lauro, Esq.  
Reg. No. 32,360  
P.O. Box 55874  
Boston, MA 02205  
(617) 517-5509

Date: March 31, 2004

**Customer No.: 21874**

APPLICANT FACSIMILE OF FORM PTO-1449

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APPLICANT

King, K. et al.

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LIST OF PUBLICATIONS CITED BY APPLICANT  
(Use several sheets if necessary)

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A1	4,546,082	10/85	Kurjan et al.	435	172.3	
	A2	4,615,974	10/86	Kingsman et al.	435	68	
	A3	4,775,622	10/88	Hitzeman et al.	435	68	
	A4	4,797,359	01/89	Finkelstein	435	68	
	A5	4,865,989	09/89	Hitzeman et al.	435	320	
	A6	4,876,197	10/89	Burke et al.	435	172.3	
	A7	4,880,734	11/89	Burke et al.	435	68	

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		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	A8	0 123 544	10/84	EPO				
	A9	WO 90/05780	05/90	PCT				
	A10	WO 91/01379	02/91	PCT				
	A11	WO 91/12273	08/91	PCT				

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	A12	Bouvier, M. et al. "Expression of a Human cDNA Encoding the $\beta_2$ -Adrenergic Receptor in Chinese Hamster Fibroblasts (CHW): Functionality and Regulation of the Expressed Receptors," <i>Molecular Pharmacology</i> 33:133-139 (1987)
	A13	Bunzow, J. et al. "Cloning and Expression of a Rat D <sub>2</sub> Dopamine Receptor cDNA," <i>Nature</i> 336:783-787 (1988)
	A14	Burkholder et al. "The yeast $\alpha$ -factor receptor: structural properties deduced from the sequence of the STE2 gene," <i>Nucleic Acids Research</i> 13(23):8463-8475 (1985)
	A15	Chen, William S. et al. "Requirement for Intrinsic Protein Tyrosine Kinase in the Immediate and Late Actions of the EGF Receptor," <i>Nature</i> 328(27):820-823 (1987)
	A16	Chen, Y. et al. "Shc Adaptor Proteins are Key Transducers of Mitogenic Signaling Mediated by the G Protein-coupled Thrombin Receptor," <i>The EMBO Journal</i> 15(5):1037-1044 (1996)
	A17	Collins, Sheila et al. "cAMP Response Element In The $\beta_2$ -Adrenergic Receptor Gene Confers Transcriptional Autoregulation by cAMP," <i>The Journal of Biological Chemistry</i> 265(31):19330-19335 (1990)
	A18	Collins, Sheila et al. "cAMP Stimulates Transcription of the $\beta_2$ -adrenergic Receptor Gene In Response To Short-Term Agonist Exposure," <i>Proc. Natl. Acad. Sci. USA</i> 86:4853-4857 (1989)
	A19	Colton, Douglas et al. "Development of An Assay for H <sub>2</sub> -Receptor Antagonists Using Isolated Fat Cells," <i>Journal of Pharmacological Methods</i> 3:253-266 (1980)
	A20	Comb, Michael et al. "A Cyclic AMP-And Phorbol Ester-Inducible DNA Element," <i>Nature</i> 323(25):353-356 (1986)
	A21	Condorelli, D.F. et al. "Induction of Protooncogene FOS by Extracellular Signals in Primary Glial Cell Cultures," <i>Journal of Neuroscience Research</i> 23:234-239 (1989)
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.		

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	B1	4,952,499	08/90	Cantor et al.	435	172.3	
	B2	5,071,773	12/91	Evans et al.	436	501	
	B3	5,215,915	06/93	Tiberi et al.	435	252.3	
	B4	5,242,822	09/93	Marullo et al.	435	252.3	
	B5	5,245,011	09/93	Tiberi et al.	530	350	
	B6	5,284,746	02/94	Sledziewski et al.	435	6	
	B7	5,310,662	05/94	Evans et al.	435	64.1	

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							YES	NO
	B8	WO 91/15583	10/91	PCT				
	B9	WO 92/10583	06/92	PCT				
	B10	WO 92/19723	11/92	PCT				

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	B11	Coso, O. et al. "Signaling from G Protein-coupled Receptors to c-Jun Kinase Involves $\beta\gamma$ Subunits of Heterotrimeric G Proteins Acting on a Ras and Rac1-dependent Pathway," <i>The Journal of Biological Chemistry</i> 271(8):3963-3966 (1996)
	B12	Damante, Giuseppe et al. "IGF-I Increases C-FOS Expression In FRTL5 Rat Thyroid Cells By Activating The C-FOS Promoter," <i>Biochemical and Biophysical Research Communications</i> 151(3):1194-1199 (1988)
	B13	Deschamps, Jacqueline et al. "Identification of a Transcriptional Enhancer Element Upstream from the Proto-Oncogene fos," <i>Science</i> 230:1174-1177 (1985)
	B14	Deutsch, Paul J. et al. "Cyclic AMP and Phorbol Ester-Stimulated Transcription Mediated by Similar DNA Elements That Bind Distinct Proteins," <i>Proc. Natl. Acad. Sci. USA</i> 85:7922-7926 (1988)
	B15	Dhanasekaran, N. et al. "G Protein-coupled Receptor Systems Involved in Cell Growth and Oncogenesis," <i>Endocrine Reviews</i> 16(3):259-270 (1995)
	B16	Dietzel, Christine et al. "The Yeast SCG1 Gene: A G $\alpha$ -like Protein Implicated in the a- and $\alpha$ -Factor Response Path," <i>Cell</i> 50:1001-1010 (1987)
	B17	Dohlman, H. et al., "Inhibition of G-Protein Signaling by Dominant Gain-of-Function Mutations in Sst2p, a Pheromone Desensitization Factor in <i>Saccharomyces cerevisiae</i> ," <i>Molecular and Cellular Biology</i> , vol. 15, no. 7, 3635-3643 (1995);
	B18	Emorine, L.J. et al. "Structure of the Gene for Human $\beta_2$ -Adrenergic Receptor: Expression and Promoter Characterization," <i>Proc. Natl. Acad. Sci. USA</i> 84:6995-6999 (1987)
	B19	Felder, Christian et al. "A Transfected m1 Muscarinic Acetylcholine Receptor Stimulates Adenylate Cyclase via Phosphatidylinositol Hydrolysis," <i>The Journal of Biological Chemistry</i> 264(34):20356-20362 (1989)
	B20	Finn, Frances M. et al. "Binding and Autophosphorylating Activity of Human Insulin Analogs," <i>Biol. Chem. Hoppe-Seyler</i> 370:559-564 (1989)
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	C1	5,352,660	10/94	Pawson	514	12	
	C2	5,364,791	11/94	Vegeto et al.	435	320.1	
	C3	5,369,028	11/94	Harpold	435	252.3	
	C4	5,378,603	01/95	Brown et al.	435	6	
	C5	5,384,243	01/95	Gutkind et al.	435	6	
	C6	5,386,025	01/95	Jay et al.	536	23.5	
	C7	5,389,543	02/95	Bunzow et al.	435	252.3	

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	C8	Fraser, Claire et al. "Cloning, Sequence Analysis, and Permanent Expression of A Human $\alpha_2$ -Adrenergic Receptor In Chinese Hamster Ovary Cells," <i>The Journal of Biological Chemistry</i> 264(20):11754-11761 (1989)
	C9	Fujita, N. et al. "Biosynthesis of the Torpedo californica Acetylcholine Receptor $\alpha$ Subunit in Yeast," <i>Science</i> 231:1284-1287 (1986)
	C10	George, Shaji et al. "Receptor Density and cAMP Acculation: Analysis In CHO Cells Exhibiting Stable Expression of A cDNA That Encodes The Beta <sub>2</sub> -Adrenergic Receptor," <i>Biochemical and Biophysical Research Communications</i> 150(2):665-672 (1988)
	C11	Gubits, Ruth et. al. "Adrenergic Receptors Mediate Changes In c-FOS mRNA Levels In Brain," <i>Molecular Brain Research</i> 6:39-45 (1989)
	C12	Hadcock, John et al. "Down-Regulation of $\beta$ -Adrenergic Receptors: Agonist-Induced Reduction In Receptor mRNA Levels," <i>Proc. Natl. Acad. Sci. USA</i> 85:5021-5025 (1988)
	C13	Hempstead, Barbara et al. "Expression of Functional Nerve Growth Factor Receptors After Gene Transfer," <i>Science</i> 243:373-375 (1989)
	C14	Huang, H. et al. "Functional Expression of Rat M5 Muscarinic Acetylcholine Receptor in Yeast," <i>Biochemical and Biophysical Research Communications</i> 182(3):1180-1186 (1992)
	C15	Jahng, Kwang-Yeop et al., "Mutations in a Gene Encoding the $\alpha$ Subunit of a <i>Saccharomyces cerevisiae</i> G Protein Indicate a Role in Mating Pheromone Signaling," <i>Molecular and Cellular Biology</i> 8(6):2484-2493 (1988)
	C16	Kang, Yoon-Se et al., "Effects of Expression of Mammalian G $\alpha$ and Hybrid Mammalian-Yeast G $\alpha$ Proteins on the Yeast Pheromone Response Signal Transduction Pathway," <i>Molecular and Cellular Biology</i> 10(6):2582-2590 (1990)
	C17	Kao, L. et al. "Interactions Between the Ankyrin Repeat-Containing Protein Akr1p and the Pheromone Response Pathway in <i>Saccharomyces cerevisiae</i> ," <i>Molecular and Cellular Biology</i> 16(1):168-178 (1996)
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<b>LIST OF PUBLICATIONS CITED BY APPLICANT</b> (Use several sheets if necessary)	APPLICANT <b>King, K. et al.</b>	
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	D1	5,401,629	03/95	Harpold et al.	435	6
	D2	5,407,820	04/95	Ellis et al.	435	240.2
	D3	5,426,177	06/95	Davis et al.	530	395
	D4	5,436,128	07/95	Harpold et al.	435	6
	D5	5,468,615	11/95	Chio et al.	435	7.2
	D6	5,482,835	01/96	King et al.	435	6
	D7	5,576,210	11/96	Sledziewski et al.	435	254.21

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D8	King, K. et al. "Control of Yeast Mating Signal Transduction by a Mammalian $\beta_2$ -Adrenergic Receptor and $G_s$ $\alpha$ Subunit," <i>Science</i> 250:121-123 (1990)
D9	Kingsman, S.M. et al. "The Production of Mammalian Proteins in <i>Saccharomyces cerevisiae</i> ," <i>TIBTECH</i> 5:53-57 (1987)
D10	Kobilka, Brian K. et al. "Functional Activity and Regulation of Human $\beta_2$ -Adrenergic Receptors Expressed in <i>Xenopus</i> Oocytes," <i>The Journal of Biological Chemistry</i> 262(32):15796-15802 (1987)
D11	Kousvelari, Eleni et al. "Regulation of Proto-Oncogenes In Rat Parotid Acinar Cells in Vitro After Stimulation of $\beta$ -Adrenergic Receptors," <i>Experimental Cell Research</i> 179:194-203 (1988) (abstract only)
D12	Kronstad, J.W. et al., "A Yeast Operator Overlaps an Upstream Activation Site," <i>Cell</i> 50:369-377 (1987)
D13	Lefkowitz, Robert J. et al. "The New Biology of Drug Receptors," <i>Biochemical Pharmacology</i> 38(18):2941-3948 (1989)
D14	Lesueur, Laurence et al. "Prolactin Stimulates Milk Protein Promoter In CHO Cells Cotransfected With Prolactin Receptor cDNA," <i>Molecular and Cellular Endocrinology</i> 71:R7-R12 (1990)
D15	Levitzki, Alexander, "From Epinephrine to Cyclic AMP," <i>Science</i> 241:800-806 (1988)
D16	Mahadevan, M. et al. "Short Communication: Isolation of a Novel G Protein-Coupled Receptor (GPR4) Localized to Chromosome 19q13.3," <i>Genomics</i> 30:84-88 (1995)
D17	Marullo, Stefano et al., "Expression of Human $\beta_1$ and $\beta_2$ Adrenergic Receptors in <i>E. coli</i> as a New Tool for Ligand Screening," <i>Bio/Technology</i> 7:923-927 (1989)
D18	Matsui, Toshimitsu et al. "Independent Expression of Human $\alpha$ or $\beta$ Platelet-Derived Growth Factor Receptor cDNAs in a Naive Hematopoietic Cell Leads to Functional Coupling with Mitogenic and Chemotactic Signaling Pathways," <i>Proc. Natl. Acad. Sci. USA</i> 86:8314-8318 (1989)
D19	Mechti, Nadir et al. "Sequence Requirements for Premature Transcription Arrest Within The First Intron of the Mouse c-fos Gene," <i>Molecular and Cellular Biology</i> 11(5):2832-2841 (1991)

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	E1	5,618,720	04/97	Ellis et al.	435	325	
	E2	5,665,543	09/97	Fowlkes	435	6	
	E3	5,739,029	04/98	King et al.	435	254.21	

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	E4	Mei, Lin et al. "Pharmacological Characterization of the M <sub>1</sub> Muscarinic Receptors Expressed In Murine Fibroblast B82 Cells," <i>The Journal of Pharmacology and Experimental Therapeutics</i> 248(2):661-670 (1989)
	E5	Miyajima, Ikuko et al., "GPA1, A Haploid-Specific Essential Gene, Encodes a Yeast Homolog of Mammalian G Protein Which May Be Involved in Mating Factor Signal Transduction," <i>Cell</i> 50:1011-1019 (1987)
	E6	Nagayama, Y. et al., "Involvement of G Protein-coupled Receptor Kinase 5 in Homologous Desensitization of the Thyrotropin Receptor," <i>The Journal of Biological Chemistry</i> 271(17):10143-10148 (1996)
	E7	Nakayama, N. et al., "Nucleotide sequences of STE2 and STE3, cell type-specific sterile genes from <i>Saccharomyces cerevisiae</i> ," <i>The EMBO Journal</i> 4(10):2643-2648 (1985)
	E8	Neve, Kim A. et al. "Functional Characterization of a Rat Dopamine D-2 Receptor cDNA Expressed in a Mammalian Cell Line," <i>The American Society for Pharmacology and Experimental Therapeutics</i> 36:446-451 (1989)
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	E11	Regan, J.W. et al. "Cloning and Expression of a Human Kidney cDNA for an $\alpha_2$ -Adrenergic Receptor Subtype," <i>Proc. Natl. Acad. Sci. USA</i> 85:6301-6305 (1988)
	E12	Rosenfeld, Michael G. et al., "Developmental and Hormonal Regulation of Neuroendocrine Gene Transcription," <i>Recent Progress in Hormone Research</i> 43:449-534 (1987)
	E13	Sassone-Corsi, Paolo et al. "Induction of Proto-Oncogene fos Transcription Through The Adenylate Cyclase Pathway: Characterization of a cAMP-Responsive Element," <i>Genes and Development</i> 2:1529-1538 (1988)
	E14	Sheng, Morgan et al. "Calcium and Growth Factor Pathways of c-fos Transcriptional Activation Require Distinct Upstream Regulatory Sequences," <i>Molecular and Cellular Biology</i> 8(7):2787-2796 (1988)
	E15	Siekevitz, Miriam et al. "Activation of the HIV-1 LTR by T Cell Mitogens and the Trans-Activator Protein of HTLV-I," <i>Science</i> 238:1575-1578 (1987)
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APPLICANT FACSIMILE OF FORM PTO-1449 REV. 7-98 <b>OTPE</b> <b>LIST OF PUBLICATIONS CITED BY APPLICANT</b> (Use several sheets if necessary) <b>MAR 31 2004</b>		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY DOCKET NO <b>50370-60735DIV</b>	SERIAL NO. <b>09/752,145</b>
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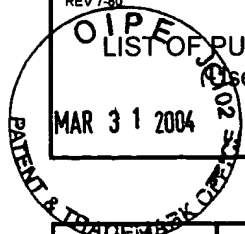
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F3	Squinto, S.P. et al. "Platelet-Activating Factor Stimulates a Fos/Jun/AP-1 Transcriptional Signaling System in Human Neuroblastoma Cells," <i>Journal of Neuroscience Research</i> 24:558-566 (1989)
F4	Stein, Reuven et al. "Cloned M1 Muscarinic Receptors mediate Both Adenylate Cyclase Inhibition and Phosphoinositide Turnover," <i>The EMBO Journal</i> 7(10):3031-3035 (1988)
F5	Stevenson, B. et al. "Mutation of RGA1, which Encodes a Putative GTPase-activating Protein for the Polarity-establishment Protein Cdc42p, Activates the Pheromone-response Pathway in the Yeast <i>Saccharomyces cerevisiae</i> ," <i>Genes &amp; Development</i> 9:2949-2963 (1995)
F6	Stryer, L. "G Proteins: A Family of Signal Transducers," <i>Ann. Rev. Cell Biol.</i> 2:391-419 (1986)
F7	Stumpo, et al. "Identification of c-fos, Sequences Involved in Induction by Insulin and phorbol Esters," <i>J. Biol. Chem.</i> 263:1611-1614 (1988)
F8	Tong-Starksen, Sandra E. et al. "Human Immunodeficiency Virus Long Terminal Repeat Responds To T-Cell Activation Signals," <i>Proc. Natl. Acad. Sci. USA</i> 84:6845-6849 (1987)
F9	Trueheart, J. et al. "Two Genes Required for Cell Fusion During Yeast Conjugation: Evidence for a Pheromone-Induced Surface Protein," <i>Molecular and Cellular Biology</i> 7(7):2316-2328 (1987)
F10	Usui, Takeshi et al. "Cyclic AMP-Responsive Region of the Human Proopiomelanocortin (POMC) Gene," <i>Molecular and Cellular Endocrinology</i> 62:141-146 (1989)
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APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-99 <b>U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE</b>	ATTY DOCKET NO <b>50370-60735DIV</b>	SERIAL NO. <b>09/752,145</b>
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APPLICANT <b>Kina. K. et al.</b>		GROUP <b>1645</b>
FILING DATE <b>December 29, 2000</b>		



## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	G1	5,747,336	05/98	Bonner, et al.			

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	G2	0 244 221 B1	11/87	EPO				
	G3	WO 88/031168	10/87	PCT				

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	G4	Blackshear et al. "Protein Kinase C-dependent and -independent Pathways of Proto-oncogene Induction in Human Astocytoma Cells" <i>The Journal of Biological Chemistry</i> 262(16):7774-4481 (1987)
	G5	Hagen, D.C. et al. "Evidence the Yeast STE3 Gene Encodes a Receptor for the Peptide Pheromone a Factor: Gene Sequence and Implications for the Structure of the Presumed Receptor" <i>Proceedings of the National Academy of Sciences of the United States of America</i> 83(5):1418-22 (1986)
	G6	Lester, H.A. "Heterologous Expression of Excitability Proteins: Route to More Specific Drugs?" <i>Science</i> 241:1057-63 (1988)
	G7	Marsh, L. et al. "STE2 Protein of <i>Saccharomyces kluyveri</i> is a Member of the Rhodopsin/ $\beta$ -adrenergic Receptor Family and is Responsible for Recognition of the Peptide Ligand $\alpha$ Factor" <i>Proceedings of the National Academy of Sciences of the United States of America</i> 85(11):3855-9 (1988)
	G8	Peralta et al. "Distinct Primary Structures, Ligand-Binding Properties and Tissue-specific Expression of Four Human Muscarinic Acetylcholine Receptors" <i>The EMBO Journal</i> 6:3923-29 (1987)
Examiner		Date Considered
*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.		

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